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EXAMINER
WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
1635	22

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/732,169	Applicant(s) HENDERSON ET AL.	
	Examiner Brian Whiteman	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/18/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8,55-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-8,55-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *1/2/03* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Non-Final Rejection

Claims 1, 3-8, and 55-80 are pending.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/18/03 has been entered.

Information Disclosure Statement

Each U.S. Patent cited on the IDS in paper no. 8 filed on 1/10/02 was considered and initialed on the 1449 by the examiner. However, if the application was allowed the U.S. patents would not be printed on the patent. If the applicants want the US Patents to be printed should the application be in condition for allowance, the applicants should submit a 1449 listing the class/subclass for each US Patent listed on the 1449 filed on 1/10/02.

Double Patenting

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time-wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-8, 59, 61, 67, and 77-80 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable as that of claims 1-8, 28-31, 33-34, 42, and 44-45 of co-pending Application No. 09/151,376. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Applicants' arguments filed 3/18/03 have been fully considered but they are not persuasive because applicants have not provided a terminal disclaimer.

Claims 1, 3-6, 8, 59, 61, 67, 77-80 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable as that of claims 1, 3-6, 8-9, and 12 of US Patent No. 5,698,443. For example, claim 5, of patent '443 is drawn to an adenovirus vector comprising at least one of the genes E1A, E1B, or E4 under transcription control of a prostate cell specific response element.

Applicants' arguments filed 3/18/03 have been fully considered but they are not persuasive because applicants have not provided a terminal disclaimer.

Claims 1, 3-5, 7-8, 59, 61-62, 64-69, and 71-80 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable as that of claims 1-5, 12-14, 21-23, and 27-32 of U.S. Patent No. 5,871,726. The claims 1-4, 12-13, 21-23, and 27-32 of

patent '726 are drawn to an adenovirus vector comprising an adenovirus gene essential for propagation under transcriptional control of a prostate specific response element, said prostate cell specific response element comprising an enhancer specific for prostate specific for prostate specific antigen and a promoter or the adenovirus described above further comprising a transgene, wherein the transgene under transcriptional control of a prostate specific response element (column 41 and 42, claims 1-3). In addition, the claims of the patent are drawn to an in vitro cell comprising either vector described above (column 43, claims 12-14). Furthermore, the claims of the patent are drawn to a method of propagating either adenovirus vector described above into a tumor cell (column 43, claims 21-22) or a method of suppressing tumor growth comprising introducing the either adenovirus vector described above into a tumor cell (column 44, claims 27-32). The claims 21-23, and 27-32 of patent '726 are drawn to a method of propagating either adenovirus vector described above into a tumor cell (column 43, claims 21-22) or a method of suppressing tumor growth comprising introducing the either adenovirus vector described above into a tumor cell (column 44, claims 27-32).

Although the conflicting claims in the instant application and patent '726, are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patent uses the adenovirus vector encompassed in the instant application. The difference between the claims of the instant application and patent '726 is that the application encompasses the adenovirus vector that is used in the methods of patent '726. Therefore, the claims of the instant application and patent '726 are obvious variants of one another.

Applicants' arguments filed 3/18/03 have been fully considered but they are not persuasive because applicants have not provided a terminal disclaimer.

Claims 1, 3-5, 7, 59, 61, 64, 67-68, and 71-80 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 14-16, 18, 20, 23-27, 30, 32, and 37-38 of U.S. Patent No. 6, 197,293. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims 1-6, 12, 14-16, 18, 20, 23-27, 30, 32, and 37-38 of patent '293 are drawn to a replication competent adenovirus vector comprising an adenovirus gene under transcriptional control of a probasin transcriptional regulatory element (PB-TRE), wherein the adenoviral gene is essential for replication (claims 1-6 and 23-26) and a host cell comprising the adenovirus vector (claim 16). In addition, the claims of the patent are drawn to the vector described above further comprising a heterologous gene under transcriptional control of PB-TRE (claims 15, 37-38). The claims 14, 18, 30, and 32 of patent '293 are drawn to a method for propagating the vector in cells (claims 18 and 30). The claims of the patent are also drawn to a method of suppressing tumor growth by contacting tumor cells the vector (claims 20 and 32).

Although the conflicting claims in the instant application and patent '293, are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patents use the adenovirus vector encompassed in the instant application. The difference between the claims of the instant application and patent '293 is that the application encompasses the adenovirus vector that is used in the methods of patent '293.

Therefore, the claims of the instant application and patent '293 are obvious variants of one another.

Applicants' arguments filed 3/18/03 have been fully considered but they are not persuasive because applicants have not provided a terminal disclaimer.

Claims 1, 3-5, 56-59, 61-66, 68-73, and 77-80 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-6, 11, and 37 of US Patent No. 6,254,862. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims 1, 3-6, 11, and 37 of patent '862 are drawn to a replication competent adenovirus vector comprising E1A and E1B wherein E1A and E1B are both under transcriptional control of separate alpha fetoprotein transcription elements (AFP-TRE), wherein at least one AFT TRE comprises either an enhancer or a promoter from an AFP gene (claims 1, 3-6) and a host cell comprising the vector described above (claim 11). In addition, the claims of the patent are drawn to a method of suppressing tumor growth in an individual be contacting a tumor cell with the adenovirus vector (claim 37).

Although the conflicting claims in the instant application and patent '862 are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patent uses the adenovirus vector encompassed in the instant application. The difference between the claims of the instant application and patent '862 is that the adenovirus in patent '862 is a replication competent adenovirus vector comprising two

adenoviral genes, which are both under control of an AFP-TRE. Therefore, the claims of the instant application and patent '862 are obvious variants of one another.

Applicants' arguments filed 3/18/03 have been fully considered but they are not persuasive because applicants have not provided a terminal disclaimer.

Claims 1, 3, 4, 7, 8, 56, 57, 58, 59, 61, 62, 63, 65, 66, 77, and 78 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 3, 4, 6, 7, 8, 9, 10, 12, 13, 16, 17 of US Patent No. 6,432,700. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims of patent '700 are drawn to a replication competent adenoviral vector for selective cytolysis of a target cell comprising a first adenovirus gene essential for replication under transcriptional control of a first heterologous transcriptional regulatory element (TRE) and at least a second adenovirus under transcriptional control of a second heterologous TRE, wherein the first and second heterologous TREs are cell-specific and an isolated cell comprising the adenoviral vector.

Although the conflicting claims in the instant application and patent '700 are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patent uses the adenovirus vector encompassed in the instant application. The difference between the claims of the instant application and patent '700 is that the adenovirus in patent '700 is a replication competent adenovirus vector comprising two heterologous TREs controlling two different adenovirus genes. Therefore, the claims of the instant application and patent '700 are obvious variants of one another.

Applicants' arguments filed 3/18/03 have been fully considered but they are not persuasive because applicants have not provided a terminal disclaimer.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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Claims 1, 3, 4, 6, and 55-80 are rejected under 35 U.S.C. 102(e) as being anticipated by Gregory et al. (US2001/0053768, filing date 5/3/95). Gregory teaches a method of treating mammalian cancer cells, comprising administering a replication competent adenoviral vector comprising a therapeutic gene and a disease specific gene regulatory region operationally linked to at least one replication gene wherein the cancer cells activate the tumor specific gene regulatory region causing the adenoviral to replicate (page 7, claim 1). Furthermore, Gregory teaches using the alpha-fetoprotein promoter/enhancer, the carcinoembryonic antigen promoter/enhancer or the tyrosinase promoter/enhancer (page 7, claims 2, 4, 9, respectively). Gregory further teaches that the replication gene used for making the vector in the method described above is a viral E1 genes, E2 gene, or E4 gene (pages 2 and 7, claims 16-18).

Applicants' arguments filed 3/18/03 have been fully considered but they are not persuasive. The Declaration filed on 3/18/03 under 37 CFR 1.131 has been considered but is ineffective to overcome the 102(e) reference.

The evidence submitted is insufficient to establish a reduction to practice of the invention in this country or a NAFTA or WTO member country prior to the effective date of the 102(e) reference. The Declaration only provides reduction to practice of a replication competent adenoviral vector comprising an E1a gene under transcriptional control of a prostate specific antigen promoter (TRE-PSA). However, the TRE-PSA set forth in the Declaration is not rejected under 102(e). The material and methods set forth in the Declaration do not provide evidence that the applicants were in possession of the claimed genus of replication competent adenovirus vectors before the effective filing date of Gregory. See MPEP 715.03. The Declaration did not contemplate using the other early adenoviral genes (E1b, E2, or E4) in the claimed replication competent adenoviral vector. The Declaration does not show completion of cell lines used to grow replication competent adenoviral vectors comprising an E2 gene or E4 gene operably linked to a TRE. The possession of the replication competent adenoviral vector comprising an E1a gene operably linked to the TRE-PSA would not persuade one skilled in the art that the applicants possessed so much of the invention as is shown in the reference.

Claims 1, 3, 4, 6, and 55-80 are rejected under 35 U.S.C. 102(e) as being anticipated by Hallenbeck et al. (US Patent 5,998,205, filing date 6/7/95). Hallenbeck teaches a tissue-specific replication-conditional adenovirus vector comprising a heterologous tissue-specific transcriptional regulatory sequence operably linked to the coding region of a gene that is

essential for replication, wherein said coding region is selected from the group consisting of E1a, E1b, E2a, E2b, and E4 coding regions (columns 10 and 27-30). Hallenbeck further teaches that the promoter in the vector is selected from the group consisting of alpha-fetoprotein, DF3, tyrosinase, CEA, surfactant protein, and ErbB2 promoters. An isolated tumor cell containing a tissue-specific replicational conditional adenovirus vector, said vector comprising a heterologous tissue-specific transcriptional regulatory sequence operably linked to the coding region of a gene that is essential for replication of said vector, wherein said transcriptional regulatory sequence functions in said cell so that replication of the vector occurs in said cell, wherein said coding region is selected from the group consisting of E1 a E1b, and E2 and E4 coding regions (columns 27-30). A producer cell is provided which contains a virion produced in the cell by replication in the cell of the replication-conditional adenoviral vectors (column 16).

Applicant's arguments with respect to Claims 1, 3, 4, 5, 6, and 55-80 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 4, 6, 55, and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable by Gregory et al. (US20001/0053768, filing date 5/3/95) taken with Bohinski et al. (Mol Cell Biol, Vol. 14, 1993, abstract), Abe *et al.* (PNAS, Vol. 90, 1993, abstract), Grooteclaes et al., (Cancer Res., Vol. 54, abstract, 1994). Gregory teaches a method of treating mammalian cancer cells, comprising administering a replication competent adenoviral vector comprising a therapeutic gene and a disease specific gene regulatory region operationally linked to at least one replication gene wherein the cancer cells activate the tumor specific gene regulatory region causing the adenoviral to replicate (page 7, claim 1). Furthermore, Gregory teaches using the alpha-fetoprotein promoter/enhancer, the carcinoembryonic antigen (CEA) promoter/enhancer, or the tyrosinase promoter/enhancer (page 7, claims 2, 4, 9, respectively). Gregory further teaches that the replication gene used for making the vector in the method described above is a viral E1a or E1b gene, E2 gene, or E4 gene (page 7, claims 16-18). However, Gregory does not specifically

teach an adenovirus vector comprising an adenovirus gene under transcriptional control of a cell type specific transcriptional response element (TRE), wherein the TRE is selected from the group consisting of a DF3-TRE, a surfactant TRE, and an ErbB2-TRE.

Regarding claims drawn to specific TREs, Abe, Grooteclaes, and Bohinski teach that tissue-specific promoters including DF3, surfactant, and ErbB2 are known in the art at the time the invention was made.

It would have been obvious for one of ordinary skill in the art to have modified the adenovirus vector taught by combining Gregory with taken with Bohinski, Abe, Grooteclaes, to produce an adenovirus vector comprising an adenovirus gene under transcriptional control of a cell type specific transcriptional response element (TRE), wherein the TRE is selected from the group consisting of a DF3-TRE, a surfactant TRE, and an ErbB2-TRE. It would also have been obvious for one of ordinary skill in the art to have constructed and employed the tissue-specific-replication competent adenoviral vectors by using a known tissue-specific promoter operably linked to a viral gene necessary for adenoviral replication for expressing a cytotoxic gene in a tumor cell-specific fashion in order to target and deliver the cytotoxic gene product to tumor cells. One of ordinary skill in the art would have a reasonable expectation of success in constructing and employing the tissue-specific-replication competent adenoviral vectors, particularly since Abe, Grooteclaes, and Bohinski all teach that tissue-specific promoters including DF3, surfactant, and ErbB2 are known in the art at the time the invention was made and employed for delivery of gene products to targeted cells.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicants' arguments filed 3/18/03 have been fully considered but they are not persuasive for the reasons set forth under the response to the applicants' traversal for the 102(e) rejection anticipated by Gregory.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER